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Prevalence of diabetes mellitus in 2019 novel coronavirus: A meta-analysis

Xiang Wang *, *Shoujun Wang, Liangge Sun, Guijun Qin*

Department of Endocrinology and Metabolism, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

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ABSTRACT

Background: Since December 2019, a new strain of coronavirus named 2019 novel coronavirus (2019-nCoV) has been discovered in Wuhan. The prevalence of diabetes mellitus, which is a great public health issue leading to immunity inhibition and an increased incidence of infections, has been increasing over the past ten years. The aim of this research was to systematically assess the prevalence of diabetes mellitus among 2019-nCoV.

Methods: We searched PubMed, Embase, Web of Science and Medline for observational studies up to February 25, 2020. A random effects model or fixed-effects model was applied to evaluate the pooled prevalence of diabetes mellitus and odds ratio (OR) with 95% confidence interval (CI).

Findings: In total, nine papers met the eligibility criteria. The pooled prevalence of DM was 9% (95% CI 6%–12%). There was obvious heterogeneity (I^2 65%, p = 0.004) in the prevalence of DM in these studies. The prevalence of DM in moderate patients with 2019-nCoV was 7% (95% CI 4%–10%). The prevalence of DM in severe patients with 2019-nCoV was 17% (95% CI 13%–21%). The prevalence of DM in severe patients with 2019-nCoV was significantly higher than that in moderate patients with 2019-nCoV (OR 2.49, 95% CI 1.70 to 3.64).

Interpretation: To our knowledge, this work is the first report showing the prevalence of diabetes mellitus in patients with 2019-nCoV, which is beneficial to prevent the spread of 2019-nCoV in the future.

1. Introduction

Since late December 2019, many patients with pneumonia of unclear etiology were reported to be infected with a novel coronavirus, formerly named as 2019 novel coronavirus or 2019-nCoV and recently named as COVID-19 (coronavirus disease 2019) by the World Health Organization (WHO), in Wuhan, Hubei province, China [1,2]. Epidemiological investigation showed that most of the patients were linked to the Huanan Seafood Wholesale Market. Previous studies have showed evidence for person to person transmission of the 2019-nCoV in family and hospital settings [3–5]. Clinical features of 2019-nCoV, which appeared to be similar to SARS-CoV leading to high possibility of ICU admission and high mortality, were fever, fatigue, dry cough, shortness of breath, and acute respiratory distress syndrome (ARDS) [6]. As of March 8, 2020, 80,859 cases were identified, and 3100 death cases were recorded in China. The number of identified cases

* Corresponding author at: Department of Endocrinology and Metabolism, The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe East Road, Zhengzhou, Henan, China.
E-mail address: wangxiang801028@163.com (X. Wang).
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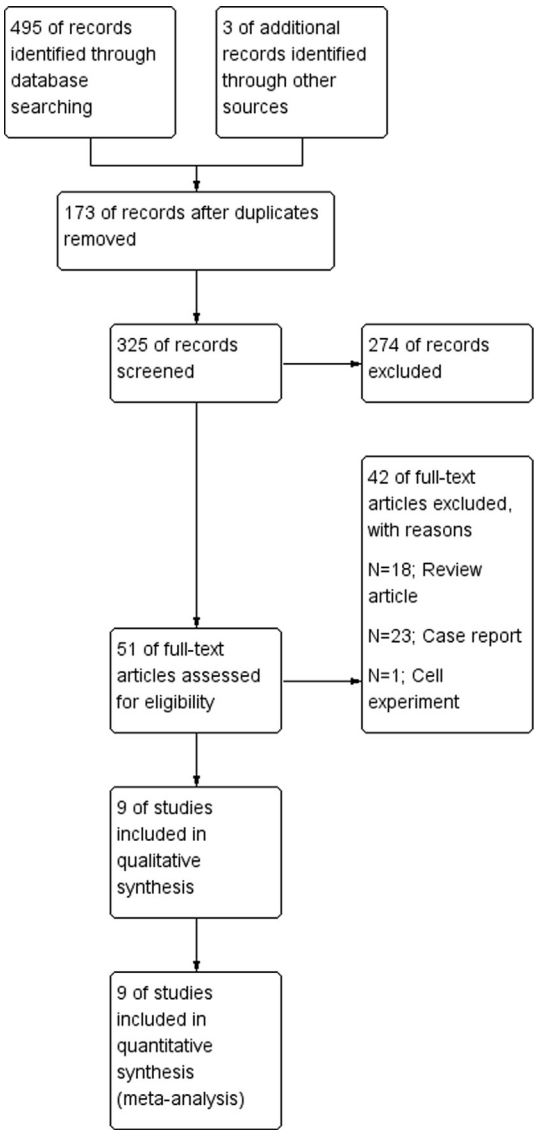

Fig. 1 – Flowchart of study selection process.

in other countries were 25208, and 532 death cases were recorded. The number of newly confirmed cases overseas is still growing, especially in South Korea, Italy, Iran, France and Germany. 2019-nCoV outbreak becomes a greater global threat than terrorism. Although the fatal rate of 2019-nCoV was less than SARS-CoV (10% mortality) and MERS-CoV (37% mortality), the confirmed cases of 2019-nCoV were higher than SARS-CoV and MERS-CoV [7–12].

Diabetes mellitus is an important global health issue leading to severe morbidity and mortality [13]. The International Diabetes Federation has anticipated that the number of diabetic patients will increase to 380 million in 2025, and will finally increase to 439 million in 2030 [13]. Previous report showed that diabetes mellitus had been linked with an increased risk of infectious disease hospitalization [14]. Former study demonstrated that the incidence of postoperative pneumonia was higher in T2DM patients than in those without this disease [15]. Another study indicated that the long-term mortality in community-acquired pneumonia among patients with undiagnosed diabetes mellitus was higher than patients without diabetes mellitus [16].

Therefore, the aims of this *meta*-analysis were to determine the prevalence of diabetes mellitus among 2019-nCoV.

2. Methods

2.1. Search strategy

A literature search was performed using PubMed, Embase, Web of Science, and Medline up to February 25, 2020 in the English language. The database searches were conducted using the following keywords: (coronavirus disease 2019 virus) or (SARS-CoV-2) or (SARS2) or (2019 novel coronavirus) or (2019-nCoV) or (2019nCoV) or (2019 novel coronavirus pneumonia) or (NCIP) or (COVID19 virus) or (COVID19-virus). Reference lists and cited articles of each paper were reviewed manually for avoiding any omission.

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) the studies were published in English; (2) 2019-nCoV diagnosed depending on World Health Organization interim guidance; (3) those were clinical studies; (4) clinical information can be collected from the articles. The exclusion criteria were as follows: (1) articles were not published in English; (2) duplicate articles, letters, editorials, non-human studies and expert opinions; (3) no eligible data for collection.

2.3. Data extraction

Two independent investigators independently examined and extracted data from the literature search, with any debate determined by mutual discussion. The following information was extracted from the selected studies: the corresponding author's name, publication year, country of origin, study design, diagnostic criteria of 2019-nCoV, the prevalence of diabetes mellitus.

2.4. Statistical analysis

Meta-analysis was performed using the STATA package version 13.1 (Stata Corporation, College Station, TX, USA) to merge the prevalence of all studies, and determine the pooled prevalence and its 95% confidence interval (CI) using the generic inverse variance method. A $\chi 2$-test-based Q statistic test at $P < 0.05$ and I2 greater than 50% was conducted to assess the between-study heterogeneity. A fixed-effects model was applied ($P \geq 0.05$ or $I2 \leq 50\%$). Otherwise, a random effect model was applied ($P < 0.05$ or I2 greater than 50%). Analysis of sensitivity was conducted to evaluate the stability of the *meta*-analysis with the metaninf algorithm in STATA. The publication bias was investigated through a visual inspection of funnel plots, Begg's rank correlation test and Egger's regression test with the meta bias algorithm in STATA. An asymmetric inverted funnel shape or $P < 0.05$ shows the possible existence of publication bias.

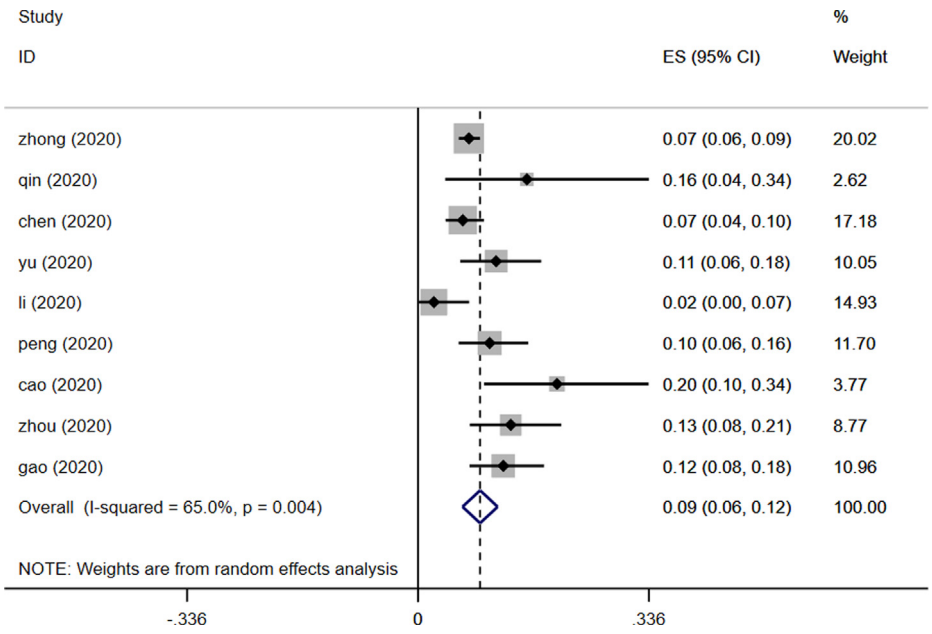

Fig. 2 – Forest plots of pooled prevalence of diabetes mellitus in 2019-nCoV Patients.

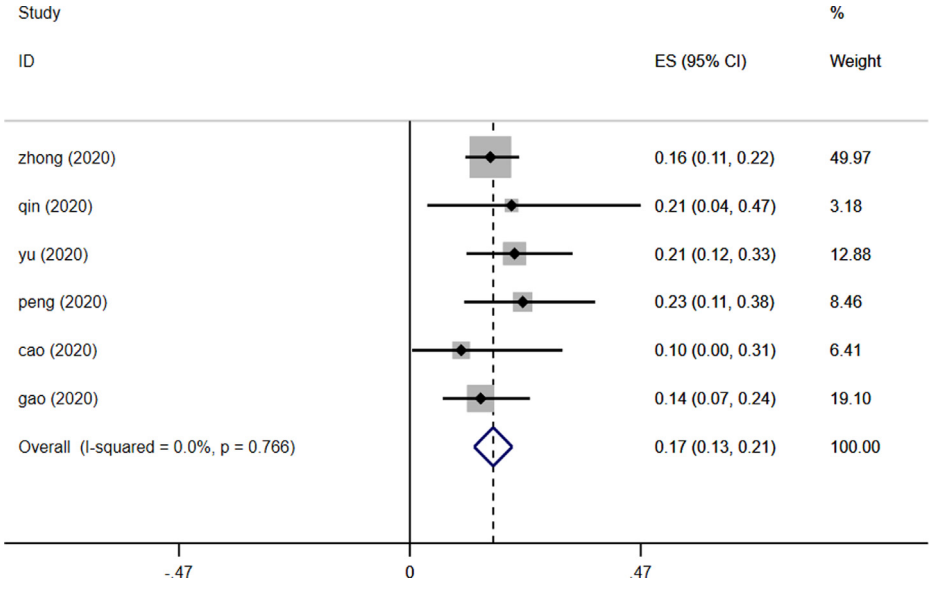

Fig. 3 – Forest plots of pooled prevalence of diabetes mellitus in severe patients with 2019-nCoV.

Table 1 – Characteristics of Included Studies.

Study, Year	Country	Type of Study	Diagnostic Method of 2019-CoV	Diabetes Prevalance
Zhong 2020	China	retrospective study	RT-PCR	7.4%
Qin 2020	China	retrospective study	RT-PCR	14.3%
Chen 2020	China	retrospective study	RT-PCR	6.4%
Yu 2020	China	retrospective study	RT-PCR	11%
Li 2020	China	retrospective study	RT-PCR	1.6%
Peng 2020	China	retrospective study	RT-PCR	10.1%
Cao 2020	China	retrospective study	RT-PCR	20%
Zhou 2020	China	retrospective study	RT-PCR	13.1%
Gao 2020	China	retrospective study	RT-PCR	12.1%

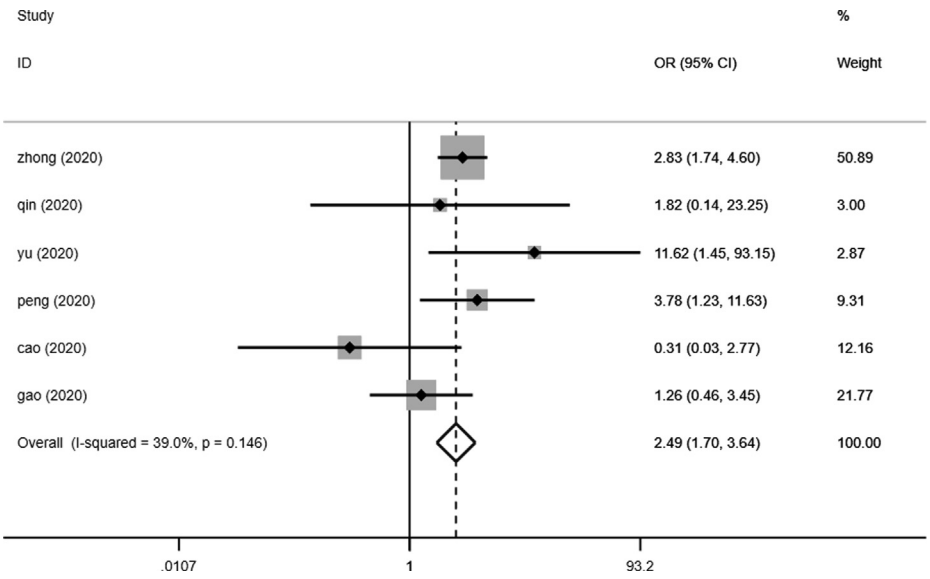

Fig. 4 – Forest plots of pooled OR of diabetes mellitus in severe patients with 2019-nCoV and moderate patients with 2019-nCoV.

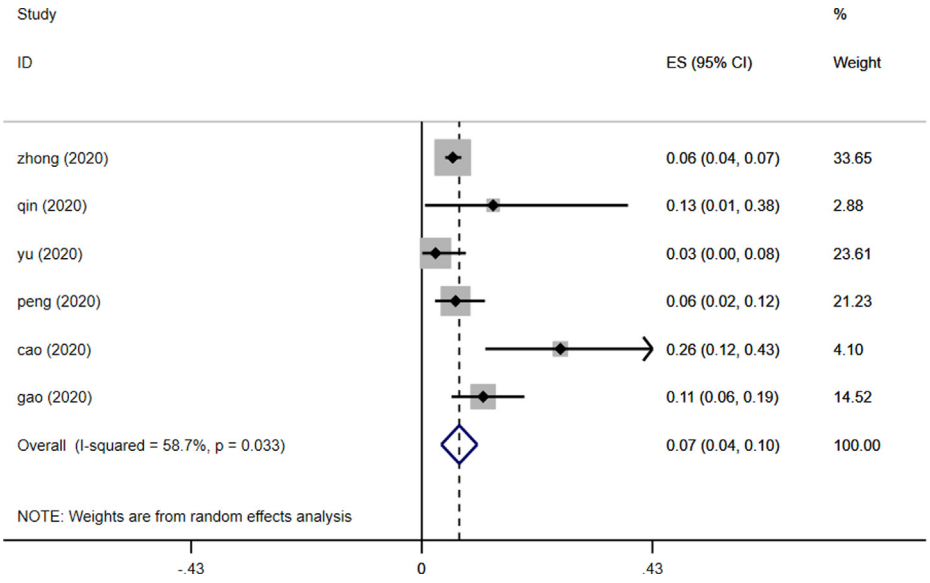

Fig. 5 – Forest plots of pooled prevalence of diabetes mellitus in moderate patients with 2019-nCoV.

3. Results

3.1. *Literature search*

We performed literature search process from PubMed, Embase, Web of Science, and Medline. 495 records were identified through the database searching and 3 additional records identified through other sources, 173 records were removed because of duplication. 325 records were screened for eligibility, 274 records were excluded after screening the titles and abstracts. After reviewing the remaining 51 records, we removed 42 records according to the reasons explained in Fig. 1. Altogether, 9 studies, which were published before Feb 25, 2020, met the inclusion criteria and were assessed in the meta-analysis (Fig. 1) [6,17–24].

3.2. *Characteristics of included studies*

The characteristics of the 9 studies were exhibited in Table 1. All included studies were retrospective in design. The diagnosis of 2019-nCoV was based on World Health Organization interim guidance in 9 studies. All included studies came from Asia (China). A total sample of 2007 patients with 2019-nCoV were included in the analysis. Among the 9 studies, the maximum number of cases was 1099, whereas the minimum was 21. 7 studies involving

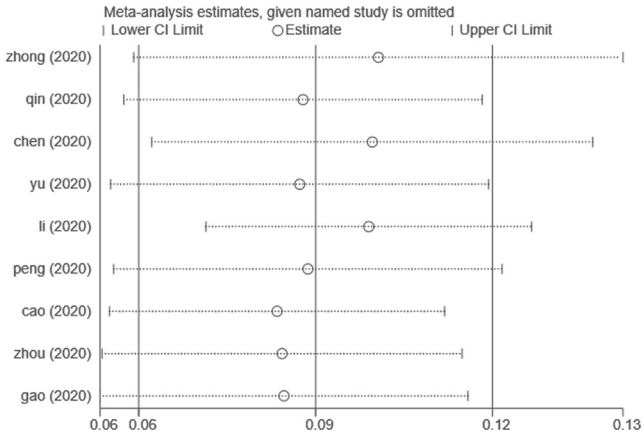

Fig. 6 – Forest plots of sensitivity of each included study.

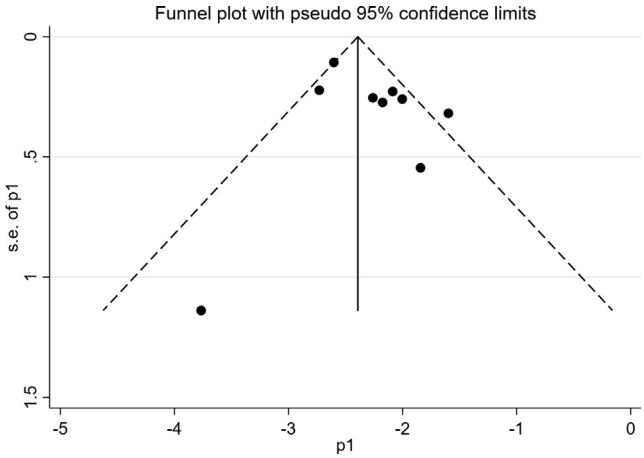

Fig. 7 – Funnel plot to detect publication bias.

more than 50 cases and 2 studies involving<50 cases among the 9 studies.

3.3. *Prevalence of DM in 2019-nCoV patients*

The pooled prevalence of DM was 9% (95% CI 6%–12%). There was obvious heterogeneity (I^2 65%, p = 0.004) in the prevalence of DM in these studies (Fig. 2). During the sensitivity analysis, the omission of any study did not have a significant influence on the combined estimates, which exhibited a relatively low sensitivity (Fig. 6). The symmetry of the funnel plot showed the absence of publication bias within studies (Fig. 7). The P values for Begg's test and Egger's test were 0.251 and 0.221, respectively.

3.4. *The prevalence of DM in severe patients with 2019-nCoV*

The prevalence of DM in severe patients with 2019-nCoV was 17% (95% CI 13%–21%). There was no obvious heterogeneity (I^2 0%, p = 0.766) in the prevalence of DM in these studies (Fig. 3). The prevalence of DM in severe patients with 2019-nCoV was significantly higher than that in moderate patients with 2019-nCoV (OR 2.49, 95% CI 1.70 to 3.64). There was no obvious heterogeneity (I^2 39%, p = 0.146) in these studies (Fig. 4).

3.5. *The prevalence of DM in moderate patients with 2019-nCoV*

The prevalence of DM in moderate patients with 2019-nCoV was 7% (95% CI 4%–10%). There was obvious heterogeneity (I^2 58.7%, p = 0.033) in the prevalence of DM in these studies (Fig. 5).

3.6. *The age difference between moderate COVID-19 group and severe COVID-19 group*

The mean age of severe COVID-19 group was 56.5 years, and the mean age of moderate COVID-19 group was 46.4 years. The mean age of moderate COVID-19 group was significantly younger than the mean age of severe COVID-19 group (-10.09, 95% CI −14.55,–5.63) (Fig. 8).

4. Discussion

Our meta-analysis has collected data from all observational studies on 2019-nCoV patients with diabetes mellitus in the world. The diagnosis of 2019-nCoV was based on World Health Organization interim guidance (by RT-PCR). The pooled prevalence of DM in 2019-nCoV Patients was 9% (95% CI, 6%–12%) in 9 eligible studies comprising a total of 2007 cases. There was obvious heterogeneity (I^2 95%, p = 0.004) in the prevalence of DM in these studies partly due to sample size, design, screening methods and diagnostic method, which was not solved by our sensitivity analyses.

The prevalence of DM is rising due to increased obesity and population ageing. There was a close relationship between diabetes and infection. Previous study showed that patients with DM were susceptible to developing infections with lower (but not upper) respiratory tract infections and urinary tract infections [25]. Another study demonstrated that patients with diabetes were more likely to be admitted to hospital with infection compared with patients without diabetes [26]. Former study showed that infections were more serious in older people with type 2 diabetes [27]. A *meta*-analysis of

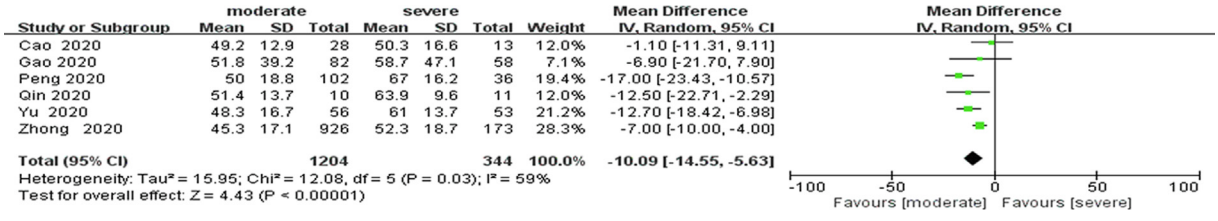

Fig. 8 – Forest plots of the age difference between moderate COVID-19 group and severe COVID-19 group.

97 prospective cohort studies showed that patients with diabetes have a higher risk of death from all causes compared with patients without diabetes [28].

Previous study demonstrated that the prevalence rates of type 2 diabetes mellitus were 7.3% (95% CI 5.8–8.7%) in 45–54 years age group, 11.0% (95% CI 9.0–13.0%) in the 55–64 years age group in China [29]. Another study showed that the age-standardized prevalence of total diabetes were 9.7% (10.6% among men and 8.8% among women), which was similar with the prevalence of DM in 2019-nCoV Patients (9% ,95% CI 6%–12%) and the overall prevalence of type 2 diabetes mellitus(9.1%) [29,30]. The prevalence of diabetes were 20.4% in the more than 60 years age group, which was slightly higher than the prevalence of DM in severe patients with 2019-nCoV whose median age were 56.5 years (17%, 95% CI 13%–21%) [30].

However, our research has some limitations. First, we did not perform subgroup analysis due to many of the included studies did not divide the participants into different groups for outcome analysis. Second, all the studies in this Meta-analysis were retrospective with obvious heterogeneity, we adopted random-effects in meta-analysis to solve this problem. Third, because our study is the single-arm meta-analysis without a control group, causality is hard to determine. Fourth, because all included studies were retrospective studies, and most of them did not have age groups. We also cannot obtain the data of the age of 2019-nCoV patients with diabetes mellitus from all included studies. We did not perform age adjustment analysis in this study.

In summary, our *meta*-analysis has demonstrated that diabetes are prevalent in patients with 2019-nCoV, especially in severe patients with 2019-nCoV . By far, this research is the first report showing the prevalence of diabetes mellitus in patients with 2019-nCoV, which is beneficial to inhibit the spread of 2019-nCoV in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

Xiang Wang had roles in the study design, data collection, data analysis, data interpretation, literature search, and writing of the manuscript. Shoujun Wang, Liangge Sun, and Guijun Qin had roles in data collection, data analysis. All authors reviewed and approved the final version of the manuscript.

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